

APPLICATION SERIAL NO. 09/719,045

AMENDMENT AND REQ. FOR RECONSIDERATION DATED APRIL 25, 2005

REPLY TO FINAL REJECTION OF MARCH 24, 2004 AND FOLLOWING

NOTICE OF APPEAL FILED ON SEPTEMBER 24, 2004

STATUS OF THE CLAIMS

The following claim listing replaces all previous listings of the claims.

Please amend the claims as indicated.

Claim 1 (**currently amended**) A divalent antibody fragment comprising two antibody heavy chains and at least one polymer molecule effective for increasing the circulating half-life of said fragment in covalent linkage, each heavy chain being covalently linked to the other by at least one non-disulphide interchain bridge linking the sulphur atom of a cysteine residue in one chain to the sulphur atom of a cysteine residue in the other chain, said cysteine residues being located outside of the variable region domain of each chain, characterised in that the at least one non-disulphide interchain bridge contains a the at least one covalently linked polymer molecule.

Claim 2 (**previously presented**) An antibody fragment according to Claim 1 in which each heavy chain is covalently linked to the other by a single non-disulphide bridge, said bridge containing a covalently linked polymer molecule effective for increasing the circulating half-life of said fragment.

Claim 3 (**previously presented**) An antibody fragment according to Claim 1 wherein each heavy chain is paired with a light chain.

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Claim 4 (**previously presented**) An antibody fragment according to Claim 1 wherein each heavy chain is a V_H -CH1 chain terminally substituted by a hinge region domain.

Claim 5 (**original**) An antibody fragment according to Claim 4 wherein each non-disulphide bridge present links the sulphur atom of a cysteine residue located in the hinge region domain of one heavy chain, to the sulphur atom of a cysteine residue in the hinge region domain of the other chain.

Claim 6 (**previously presented**) An antibody fragment according to Claim 1 wherein the polymer is an optionally substituted straight or branched chain polymer selected from the group consisting of polyalkylene, polyalkenylene and polyoxyalkylene, or a branched or unbranched polysaccharide.

Claim 7 (**previously presented**) An antibody fragment according to Claim 6 wherein the polymer is an optionally substituted straight or branched chain polymer selected from the group consisting of poly(ethylene glycol) or a derivative of poly(ethylene glycol).

Claim 8 (**withdrawn**) An antibody fragment according to Claim 7 wherein the polymer is selected from the group consisting of methoxy(polyethylene glycol) or a derivative of methoxy(polyethylene glycol).

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Claim 9 (**withdrawn**) An antibody fragment according to Claim 8 wherein the polymer has a molecular weight in the range from about 25000Da to about 40000Da.

Claim 10 (**previously presented**) An antibody fragment according to Claim 1 wherein each interchain bridge is the residue of a homo- or heterobifunctional cross-linking reagent.

Claim 11 (**original**) An antibody fragment according to Claim 10 wherein each bridge is an optionally substituted C₄₋₂₀ alkylene chain optionally interrupted by one or more heteroatoms or heteroatom-containing groups.

Claim 12 (**previously presented**) An antibody fragment according to Claim 1 which is covalently attached to one or more effector or reporter molecules.

Claim 13 (**previously presented**) An antibody fragment according to Claim 1 which is able to selectively bind to a cell surface or soluble antigen.

Claim 14 (**original**) An antibody fragment according to Claim 13 wherein the antigen is human tumour necrosis factor- α or a platelet derived growth factor or a receptor thereof.

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PATENT

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Claim 15 **(previously presented)** A pharmaceutical composition comprising an antibody fragment according to any of the preceding claims together with one or more pharmaceutically acceptable excipients, diluents or carriers.